

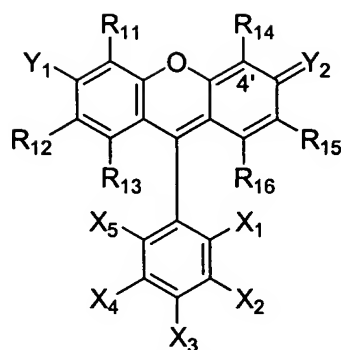
**AMENDMENTS TO THE SPECIFICATION:**

**Please replace the paragraph beginning on page 1, lines 8-13, with the following amended paragraph:**

--This application is a continuation of U.S. Application Serial No. 10/014,743, filed on October 29, 2001, which is a continuation of U.S. Application Serial No. 09/272,097, filed on March 18, 1999, now U.S. Patent No. 6,335,440, which is a continuation of U.S. Application Serial No. 09/046,203, now U.S. Patent No. 5,945,526, which is a continuation of U.S. Application Serial No. 08/726,462, filed on October 4, 1996, now U.S. Patent No. 5,800,996, which is a continuation-in-part of "ENERGY TRANSFER DYES WITH ENHANCED FLUORESCENCE," U.S. Application Serial No. 08/672,196, filed on June 27, 1996, now U.S. Patent No. 5,847,162, which is a continuation-in-part of U.S. Application Serial No. 08/642,330, filed on May 3, 1996, now U.S. Patent No. 5,633,727, each of ~~Application Serial no. 08/642,330; Filed May 3, 1996 and U.S. Application Serial No.: 08/672,196; filed June 27, 1996; entitled "4,7-DICHLORORHODAMINE DYES"~~ which are incorporated herein by reference.--

**Please replace the text of the paragraph beginning on page 10, lines 20-30, and page 11, lines 1-4, with the following amended paragraph:**

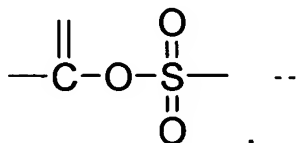
-- In another embodiment, the energy transfer fluorescent dyes have donor and acceptor dyes with the general structure



where  $Y_1$  and  $Y_2$  taken separately are either hydroxyl, oxygen, iminium or amine, the iminium and amine preferably being a tertiary iminium or amine and  $R_{11}$ -[[ $R_{17}$ ]]  $R_{16}$  are any substituents which are compatible with the energy transfer dyes of the present invention.--

**Please replace the paragraph beginning on page 53, lines 5-12, with the following amended paragraph:**

-- Figure 4A shows a generalized synthesis wherein the substituent  $X_1$  can be other than carboxylate. In the figure,  $X'$  indicates moieties which are precursors to  $X_1$ . In the method illustrated in Figure 4A, two equivalents of a 3-aminophenol derivative [[4a/4b]] 4A-A/4A-B, such as 3-dimethylaminophenol, is reacted with one equivalent of a dichlorobenzene derivative [[4c]] 4A-C, e.g., 4-carboxy-3,6,dichloro-2-sulfo benzoic acid cyclic anhydride, i.e., where the  $X_1'$  moieties of [[4c]] 4A-C are taken together are,



**Please replace the paragraph beginning on page 53, lines 14-19, with the following amended paragraph:**

--The reactants are then heated for 12 h in a strong acid, e.g., polyphosphoric acid or sulfuric acid, at 180°C. The crude dye [[4d]] 4A-D is precipitated by addition to water and isolated by centrifugation. To form a symmetrical product, the substituents of reactants [[4a]] 4A-A and [[4b]] 4A-B are the same, while to form an asymmetrical product, the substituents are different.--

**Please replace the paragraph beginning on page 53, lines 20-26, and page 54, lines 1-3, with the following amended paragraph:**

-- Figure 4B shows a generalized synthesis wherein the substituent X<sub>1</sub> is carboxylate. In the method of Figure 4B, two equivalents of a 3-aminophenol derivative [[4a/4b]] 4B-A/4B-B, such as 3-dimethylaminophenol, is reacted with one equivalent of a phthalic anhydride derivative [[4e]] 4B-E, e.g., 3,6-dichlorotrimellitic acid anhydride. The reactants are then heated for 12 h in a strong acid, e.g. polyphosphoric or sulfuric acid, at 180°C. The crude dye [[4d]] 4B-D is precipitated by addition of water and isolated by centrifugation. To form a symmetrical product, the substituents of reactants [[4a]] 4B-A and [[4b]] 4B-B are the same, while to form a asymmetrical product, the substituents are different. --

**Please replace the paragraph beginning on page 92, lines 2-15, with the following amended paragraph:**

-- The following example compares the fluorescence emission strength of a series of energy transfer dyes according to the present invention to the corresponding acceptor dye.

According to this example, each dye was attached to a ~~[[21]]~~ primer sequence (5'-TGTAACGACGGCCAGT) (~~SEQ. ID. NO.: 1~~) (SEQ ID NO: 2) with an aminohexyl linkage at the 5' end. The oligonucleotides were quantitated based on the absorbance at 260 nm, assuming an extinction coefficient of  $180,000 \text{ cm}^{-1} \text{ M}^{-1}$ . Spectra were obtained at a primer concentration of  $0.4 \mu\text{M}$  in 8M urea, 1X Tris/Borate/EDTA (TBE) buffer with 488 nm excitation. FIG. 9A provides the overlaid spectra of 5-CFB-DR110-2 and DR110-2. FIG. 9B provides the overlaid spectra of 5-CFB-DR6G-2 and DR6G-2. FIG. 9C provides the overlaid spectra of 6-CFB-DTMR-2 and DTMR-2. FIG. 9D provides the overlaid spectra of 6CFB-DROX-2 and DROX-2. --

**Please replace the paragraph beginning on page 93, lines 2-15 with the following amended paragraph:**

-- In this example, dye primer sequencing was performed on M13 (~~SEQ. ID. NO.: 2~~) (SEQ ID NO: 1) using 5-CF-TMR-2, 5-CF-B-TMR-2, 6-CF-B-DTMR-2 and DTMR-2 labeled primers. In this example, dye primer sequencing was performed according to the *ABI PRISM<sup>TM</sup> 377 DNA Sequencer User's Manual, Rev. B*, January 1995, Chapter 2 (p/n 402114, The Perkin-Elmer Corporation, Foster City, Calif.). The dye was attached to the 5' end of M13-21 primer (~~SEQ. ID. NO.: 3~~) (SEQ ID NO: 2). Equimolar solutions of each primer were mixed with the M13 (~~SEQ. ID. NO.: 2~~) (SEQ ID NO: 1) and sequenced with a single dideoxy nucleotide mixture (ddA/dNTP) and Taq FS. Plots of the resulting mixtures of oligonucleotides that were detected using 5-CF-TMR-2 and 5-CF-B-TMR-2 labeled primers are presented in FIG. 11. As can be seen from this figure, 5-CF-B-TMR-2 provides a significantly stronger signal than 5-CF-TMR-2, showing the fluorescence enhancement provided by the linker used in 5-CF-B-TMR-2.--

**Please replace the paragraph beginning on page 93, lines 23-29, and page 94 lines 1-2, with the following amended paragraph:**

-- Dye primer sequencing was performed on the M13 (~~SEQ ID NO: 2~~) (SEQ ID NO: 1) using a set of four dyes attached to the M13-21 primer (~~SEQ ID NO: 3~~) (SEQ ID NO: 2) as described in Example 5. Figure 13 is a four color plot of the dye labeled oligonucleotides produced from the sequencing. The peak for cytosine corresponds to the fluorescence of 5-CFB-DR110-2. The peak for adenosine corresponds to the fluorescence of 6-CFB-DR6g-2. The peak for guanosine corresponds to the fluorescence of 5-CFB-DTMR-2. The peak for thymidine corresponds to the fluorescence of 5-CFB-DROX-2.--

**Please replace pages 95-98 of the Specification regarding the Sequence Listing with the attached replacement pages 95-98 (enclosed as Attachment A).**

**In the 16 sheets of drawings, as filed, please replace drawing sheet 5 and drawing sheet 6 with the enclosed drawing sheet 5 and drawing sheet 6 respectively (enclosed as Attachment B).**